

## REMARKS/ARGUMENTS

### *Status of the Claims*

Claims 60-69 are pending. Claims 1-59 have been canceled. Reconsideration in view of the following remarks is respectfully requested.

### *Claim Rejections – 35 USC 103*

Claims 60-69 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kayyem et al., WO/1998/020162, in view of Shuber, US Patent No. 5,633,134. Applicants respectfully traverse.

Under 35 USC 103(a), the Examiner is required to establish a *prima facie* case as to why the differences between the claimed invention and the cited references are such that the claimed invention as a whole would have been obvious.

It appears that the Examiner is attempting to establish a *prima facie* case of obviousness by providing a motivation why one of skill in the art would combine reference teachings to arrive at the presently claimed invention. MPEP 2141(III), rationale (G). The Examiner has failed to establish a *prima facie* case of obviousness in this manner because at no point in the Examiner's analysis does the Examiner ever arrive at the presently claimed invention. Specifically, the Examiner has not shown where in the cited references is disclosed, in addition to a first label probe comprising a first ETM with a first redox potential, "a second label probe substantially complementary to said first domain, comprising a second nucleotide at said interrogation position **and a second ETM with a second redox potential.**" Even if the Examiner could specifically cite, according to this type of analysis, where to find such a second label probe, the Examiner is required to provide a **reason** why one of skill in the art would use such a second label probe comprising a second ETM with a second redox potential with the other recited elements in the recited steps to arrive at the presently claimed method. This the Examiner has not done.

The Examiner has not cited any part of any of the references that teaches a second label probe comprising a second ETM with a second redox potential. The teaching in Shuber of "multiple oligonucleotide probes with labels" is not a teaching of a second label probe comprising a second ETM with a second redox potential or of its use in the

step of contacting it with the recited electrode. The Examiner has provided no reason why the "labels" in Shuber's "multiple oligonucleotide probes with labels" would include a second ETM with a second redox potential.

The Examiner states that one of skill in the art would "use the ETM labeled oligonucleotides, as taught by Kayyem et al. with the multiple oligonucleotide probes for mutation detection, as taught by Shuber[.]" However, the Examiner has provided no reason why the "ETM" in Kayyem's "ETM labeled oligonucleotides" means an ETM with a second redox potential. Thus, combining "ETM labeled oligonucleotides" with "multiple oligonucleotide probes" *still* does not result in a second label probe comprising a second ETM with a second redox potential. Without explaining *how* combining Kayyem's "ETM labeled oligonucleotides" with Shuber's "multiple oligonucleotide probes" would lead to a second label probe comprising a second ETM with a second redox potential, the Examiner, lacking all the elements and steps of the presently claimed method, never "arrives at the presently claimed invention" in her analysis. Without arriving at the presently claimed invention, the Examiner could not have provided a reason for arriving at the presently claimed invention. The Examiner thus has failed to establish a prima facie case of obviousness according to the analysis that she has undertaken.

The Examiner states that "[a]dditionally, Kayyem teaches a first ETM label on a first oligonucleotide and a second ETM label on a second oligonucleotide where upon hybridization an electron is transferred from one ETM on the first oligonucleotide to the second ETM on the second oligonucleotide." However, even if this passage discloses "a second ETM label on a second oligonucleotide," the Examiner has provided no reasoned explanation why the second ETM has a second redox potential compared to a first ETM, *each of which is attached to an oligonucleotide probe different from another, which probes are contacted with an electrode* according to the present claims. Applicants note that in the embodiment cited by the Examiner on p. 52, lines 6-24 of Kayyem, one of the ETMs is itself an electrode (see line 7). One consequence is that in the cited embodiment, electron transfer between a first ETM and a second ETM occurs between an electrode and some other ETM. In contrast, the present claims require a first ETM with a first redox potential, an electrode, and a second ETM with a second redox potential. In view

of such differences, the Examiner has provided no reason why this passage of Kayyem helps to teach all the elements and steps of the present claims and no reason why this passage is otherwise relevant.

Finally, although the Examiner states that it would have been *prima facie* obvious "to use the ETM labeled oligonucleotides . . . with the multiple oligonucleotide probes for mutation detection," this is not the proper analysis because the combination at best results in nothing more than *an* element of the claimed method, but even the combination fails to teach *each* element of the claimed method. Instead, the Examiner may show that a claimed invention is obvious by providing "some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention." MPEP 2141(III), rationale (G). However, as stated above, the Examiner never arrives at all of the elements and steps of the presently claimed invention, and thus could not have provided the required rationale for establishing a *prima facie* case of obviousness.

#### ***Conclusion***

In view of the foregoing, it is believed that all claims now pending this application are in condition for allowance. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 442-1216.

Respectfully submitted,

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Date: \_\_\_\_\_

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